Glucocorticoids for COVID-19

Ismolilov Diyorbek
Fergana Medical Institute of Public Health Department "Internal Diseases № 1"

Abstract: The COVID-19 pandemic has affected every area of healthcare in every country in the world. The wide range of effects of the virus on all systems of the human body leads to a number of difficulties in the treatment of the disease. This article is a literature review that collects recommendations for the use of insulin in patients with COVID -19 taking glucocorticosteroids.

Keywords: COVID-19, diabetes, glucocorticosteroids, insulin, basal bolus therapy.

Introduction

COVID-19 was first reported in China in Wuhan in December 2019. As of March 1, 2021, the World Health Organization's COVID-19 dashboard had over 129 million confirmed cases of COVID-19 worldwide, including over 2.8 million deaths and over 104 million recoveries (WHO). SARS-CoV-2 is an RNA virus that can mutate. In human cells, the main entry receptor for SARS-CoV-2 is angiotensin -converting enzyme 2 (ACE2), which is highly expressed in lung alveolar cells, cardiomyocytes, vascular endothelium, and various other cell types [1]. In patients who died from complications of corona virus infection, a pathoanatomical autopsy revealed diffuse alveolar damage and infiltration of inflammatory cells with the formation of hyaline membranes in the lungs, myocardial inflammation, infiltration of liver lymphocytes, accumulation of macrophages in the brain, axonal damage, microthrombi in the glomeruli, and focal pancreatitis [2]. These data once again confirm that an acute inflammatory process occurs in the body. A retrospective study of 317 patients with laboratory-confirmed COVID-19 showed active inflammatory reactions (increased levels of interleukin-6, IL-6, and lactate dehydrogenase) within 24 hours of hospitalization, which correlated with the severity of the disease [3]. In addition, blood levels of IL-6 and lactate dehydrogenase are independent predictors of COVID-19 severity. The level of IL-6, which has pro- inflammatory properties, correlates with both the severity of the disease and coagulation parameters. IL-6, causing oxidative stress in the body, has a damaging effect, and this effect can lead to the rapid progression of metabolic disorders in COVID-19 [4]. In addition, increases in inflammatory markers such as D- dimer, ferritin, procalcitonin, CRP (C-reactive protein), and ESR (erythrocyte sedimentation rate) have been observed with COVID-19, which may increase the risk of microvascular and macrovascular complications arising from injury. endothelium [3].

Main part. It is known that any viral infection, including coronavirus, affects the human body at the cellular level and has a cytotoxic effect. As a result of this effect, inflammation factors (cytokines) are released in the body, which is a trigger of the autoimmune process [5]. Therefore, the use of glucocorticoids in severe forms of COVID-19 is quite pathogenetically justified. The randomized controlled trial (RCT) RECOVERY demonstrated that dexamethasone (6 mg daily for 10 days) in hospitalized patients with COVID-19 reduced 28-day mortality (odds ratio (OR) 0.83; 95% confidence interval [CI] 0.75-0.93), the duration of hospitalization and the need to switch to mechanical ventilation. prospective a meta-analysis of 7 RCTs further supported the benefit of corticosteroid therapy in reducing mortality in

critically ill patients with COVID-19 (pooled OR 0.66, 95% CI, 0.53-0.82) [6]. Thus, corticosteroid therapy is effective in severe COVID-19 [7]. It aims to support the central regulatory function of the activated glucocorticoid receptor α (GC-GRα). The greater the expression of glucocorticoid receptors in myeloid cells of bronchoalveolar lavage, the less pronounced neutrophilic pneumonia, an increase in the level of neutrophils, and the severity of symptoms. Translational researchin patients with ARDS (acute respiratory distress syndrome), randomized to the use of methylprednisolone, showed the restoration of cellular concentrations and function of activated GC-GRα during glucocorticoid therapy, which leads to suppression of the activity of markers of inflammation, coagulation and proliferation of fibrocytes [6]. According to the recommendations of the Chinese Thoracic Society, short-course, low- and medium-dose glucocorticoid therapy [8] in critically ill COVID-19 patients improves outcomes but increases the risk of hyperglycemia. Low-dose dexamethasone has also been shown to reduce mortality in hospitalized patients with COVID-19 who require respiratory support [9]. Several retrospective studies have focused on carbohydrate metabolism disorders during the COVID-19 pandemic. One study included 39 patients without diabetes and no history of steroid therapy who were hospitalized for laboratory-confirmed coronavirus pneumonia. Twenty of these patients (51%) had hyperglycemia that persisted throughout the hospital stay. The level of glycemia returned to normal by the end of treatment. Given the mechanism of action of steroidal anti-inflammatory drugs, it would be possible to explain the occurrence of hyperglycemia in COVID -associated pneumonia during glucocorticoid therapy precisely by the contra-insular mechanism of action of glucocorticoids [10]. However, with a coronavirus infection, all metabolic processes in the body are disrupted, including carbohydrate metabolism. Against the background of the inflammatory process, insulin resistance increases, metabolic disorders occur, which is further enhanced during a cytokine storm. In human monocytes, elevated glucose directly increases SARS-CoV-2 replication, and glycolysis supports SARS-CoV-2 replication through production of mitochondrial reactive oxygen species and activation of hypoxia-induced factor 1α. Therefore, hyperglycemia may contribute to the spread of the virus. In line with this, it has been suggested that hyperglycemia is an independent predictor of morbidity and mortality in patients with SARS [11]. Hyperglycemia is associated with worse prognosis of COVID-19 and is an independent predictor of severe disease [12]. Clinical guidelines recommend maintaining fasting glucose levels of 7.8–10 mmol /L for critically ill patients and a more stringent target of 4.4–6.1 mmol /L for patients with mild COVID-19 without significant hypoglycemia [13, 14, 15]. In addition, the direct cytotoxic effect of SARSCoV-2 on pancreatic β-cells, hepatocytes, myocytes, etc. should be taken into account. Damage to β-cells is the direct cause of the onset of insulin deficiency, a decrease in the level of one's own insulin and, as a result, hyperglycemia. Damage to hepatocytes and myocytes leads to increased insulin resistance [16]. Xiao et al . reported that of 95 patients with SARS treated with glucocorticoids at the maximum therapeutic dose, 34.7% of patients developed steroid-induced diabetes, and the maximum daily dose of methylprednisolone was the only predictor of diabetes [24]. In most patients, fasting glycemia returned to normal values after appropriate insulin therapy and after discontinuation of glucocorticoid therapy [17]. Correction of hyperglycemia during glucocorticoid therapy . In general, the starting dose of insulin therapy for hyperglycemia, identified for the first time against the background of the use of glucocorticoids for respiratory diseases, according to the recommendations of different a tors, ranges from 0.3 to 0.5 U/kg per day (Table 1).

Recommended dose of insulin depending on the dose and glucocorticoid preparation used in the treatment of COVID-19 [4]

Methyl - prednisolone, mg / day	Prednisone, mg/ day	Dexamethasone mg/ day	Hydrocortisone, mg/ day	Total dose of insulin, U/kg body weight/day
≥32	>40	≥8	≥200	0.4
24	thirty	6	150	0.3
sixteen	20	4	100	0.2
eight	ten	2	fifty	0.1

The therapy regimen is basis- bolus [18]. Authors from Slovenia [19] published a paper in February 2021 in which they presented the results of a retrospective observation of patients with pneumonia and steroid -induced hyperglycemia detected in a hospital. Glycemic control was carried out 4 times a day (before main meals and at bedtime). Based on the experience of Indian colleagues, the authors recommend using repaglinide for fasting glycemia and before meals from 7.0 to 11.1 mmol /l and at bedtime above 11.1 mmol /l, with glycemia above 11.1 mmol /l when at least 2 measurements during the day, the authors recommend starting insulin therapy according to the basal bolus regimen, with the dose of insulin depending on the dose of glucocorticoids received [20]. At the same time, 60% of the daily dose is given to basal insulin, 40% to ultrashort insulin in a ratio of 2:2:1 before breakfast, lunch and dinner. The authors recommend titrating the dose of insulin every 2-3 days by 20% with persistent hyperglycemia above 11.1 mmol / l. Indian authors, when choosing the starting dose of insulin therapy, are guided by the level of glycated hemoglobin. With HbA1c between 6.5 and 8.5%, the recommended starting dose is 0.4 U/kg (50% of the daily dose was assigned to extended insulin) with a corrective injection when using a glucocorticoid . With HbA1c above 8.5%, the daily dose of insulin at the start is calculated as 0.5 U/kg, also with a corrective injection during the use of glucocorticoids [20]. The peak of hyperglycemia during methylprednisolone therapy is observed after 4-6 hours. Therefore, to correct hyperglycemia during the administration of methylprednisolone, it is better to use NPH insulin, the action profile of which fully corresponds to the peak of hyperglycemia under the influence of methylprednisolone [21, 22, 23]. The glycemic effect of dexamethasone, which can last up to 48 hours, is best compensated for with a long-acting analog insulin (glargine or insulin detemir), which has a hypoglycemic effect for more than 24 hours [24, 25, 26, 27]. In this case, an additional injection of insulin is carried out simultaneously with the introduction of the glucocorticoid preparation. Thus, when treating COVID-19 with systemic corticosteroids, due to the high likelihood of hyperglycemia, it is necessary to intensify glycemic control and carry out its correction by choosing an insulin preparation in accordance with the profile of a particular systemic glucocorticosteroid[2]

Conclusions : - Under the influence of the cytotoxic effect of the SARS-CoV-2 virus in the body of patients, the immune system fails, destruction of pancreatic β-cells and activation of the inflammatory process, which lead to disruption of homeostasis and metabolic disorders, including carbohydrate metabolism. – Hyperglycemia is an independent predictor of increased risk of hospitalization and severe disease in patients with COVID-19. - Against the background of taking glucocorticoids, the risk of manifestation of diabetes mellitus, decompensation of the glycemic profile, as well as the occurrence of transient hyperglycemia increases. – Control and correction of glycemia, taking into account the action profile of a specific glucocorticoid, with an appropriate insulin preparation, provides an improvement in the glycemic profile and, accordingly, the outcomes of COVID-19.

Literature

1. Ахмедов, Ю. М., Ахмеджанов, И. А., Мавлянов, Ш. Х., Мавлянов, Ф. Ш., Ибрагимов, К. Н., & Курбанов, Ж. Ж. (2007). Рентгенопланиметрические методы диагностики обструктивныхуропатий у детей. *Саратовский научно-медицинский журнал*, *3*(2), 66.
2. Ахмедов, Ю. М., Курбанов, Д. Д., &Мавлянов, Ф. Ш. (2011). Прогноз исхода врожденного гидронефроза у детей. *Педиатрическая фармакология*, *8*(1), 108-111.
3. Мавлянов, Ф. Ш. (2010). Прогноз результатов хирургического лечения обструктивныхуропатий у детей. *Иновационные технологии педиатрии и детской хирургии: Материалы конгресса*, 389.
4. Мавлянов, Ф. Ш. (2018). Возможности методов визуализации уродинамики и функционального состояния почек при обструктивныхуропатиях у детей. *Журнал Биомедицины и практики*, (1), 4-9.
5. Ахмедов, Ю. М., Ахмеджанов, И. А., Ахмедов, Е. А., Мавлянов, Ф. Ш., Яцык, С. П., & Шарков, С. М. (2006). Функциональное состояние почки при врожденном гидронефрозе у детей. *Вопросы современной педиатрии*, (S), 35.
6. Мавлянов, Ф. Ш., &Мавлянов, Ш. Х. (2020). Факторы прогноза результатов лечения обструктивныхуропатий у детей. *Вестник науки и образования*, (9-3 (87)), 80-85.
7. Мавлянов, Ф. Ш., Широв, Т. Ф., Широв, Б. Ф., & Ахмедов, И. Ю. (2019). Возможности УЗИ в оценке функционального состояния почек у детей с врожденнымиобструктивнымиуропатиями. *Вопросы науки и образования*, (33 (83)), 74-85.
8. Мустафакулов, И. Б., Хаджибаев, А. М., &Мавлянов, Ф. Ш. (2016). Наш опыт хирургического лечения повреждений желудка при сочетанной травме. *Клінічнаанатомія та оперативна хірургія*, (15,№ 1), 71-73.
9. Мавлянов, Ф. Ш., Ахмедов, Ю. М., &Яцык, С. П. (2015). Причины неудовлетворительных результатов реконструктивно-пластических операций при врожденных обструктивныхуропатиях у детей. *Журнал теоретической и клинической медицины*, (5), 78-81.
10. Ахмедов, Ю. М., Шарков, С. М., &Мавлянов, Ф. Ш. (2004). Рентгенпланометрические исследования при врожденном гидронефрозе у детей. *Медицинский научный и учебно-методический журнал*, *20*, 86-94.
11. Мавлянов, Ф. Ш., Ахмедов, Ю. М., Мавлянов, Ш. Х., &Ахмеджанов, И. А. Способы уретероцистоанастомоза у детей с врожденныммегауретером. *В сборнике представлены современные результаты клинических и научных исследова-ний в области детской хирургии. Предназначен для врачей всех специальностей, врачей об-щей практики, студентов медицинских университетов.*, 130.
12. Мавлянов, Ш. Х., Мавлянов, Ф. Ш., Ахмедов, Ю. М., & Ганиев, Ж. А. (2020). Наша тактика в лечении ущемленных паховых грыж у детей. *Российский вестник детской хирургии, анестезиологии и реаниматологии*, *10*(S), 99-99.
13.]Шамсиев, А. М., Юсупов, Ш. А., &Шарипов, Р. Х. (2001). Влияние озонотерапии на показатели перекисного окисления липидов у детей с распространенными формами аппендикулярного перитонита. *Анналы хирургии*, (5), 77.

14. Шарипов, Р. Х. (1995). Влияние экологической обстановки крупного промышленного города на течение беременности и родов у женщин и адаптационного периода у новорожденных. *Российский вестник перинатологии и педиатрии*, *40*(6), 46.
15. Шарипов, Р., Ахмедова, М., Ирбутаева, Л., Расулов, А., & Расулова, Н. (2017). Бронхообструктивный синдром и методы коррекции у детей. *Журнал вестник врача*, *1*(1), 53-55.
16. Расулова, Н., Шарипов, Р., Расулов, А., Ахмедова, М., &Ирбутаева, Л. (2017). Взаимосвязь факторов риска развития рахита с уровнем 25 (он) d 3 в сыворотке крови у детей. *Журнал вестник врача*, *1*(1), 41-44.
17. Ахмедова, М. М., Шарипов, Р. Х., Расулова, Н. А., Расулов, А. С., &Ирбутаева, Л. Т. (2019). Дифференциальная диагностика поражения почек обменного генеза у детей раннего возраста. *Достижения науки и образования*, (12 (53)), 37-40.
18. Расулова, Н. А., Расулов, А. С., Шарипов, Р. Х., Ахмедова, М. М., &Ирбутаева, Л. Т. (2019). Оценка значимости уровня 25 (он) d3 в сыворотке крови и его влияние на профилактику рахита у детей 1-го года жизни. *Достижения науки и образования*, (11 (52)), 45-49.
19. Шарипов, Р. Х. (1994). Влияние внешней среды на здоровье новорожденных детей: Автореф. дис. д-ра мед.наук.
20. Шарипов, Р. Х., Ахмедова, М. М., Расулова, Н. А., Расулов, А. С., &Ирбутаева, Л. Т. (2019). Сравнительная оценка эффективности бронходилятаторов при обструктивных состояниях у детей. *Достижения науки и образования*, (11 (52)), 91-93.
21. Свиридов, С. В., Шарипов, Р. Х., Бакушин, В. С., Генерозова, В. Б., Федоров, С. В., Карпов, А. В., &Спивак, М. Б. (2011). Роль эпидуральной анальгезии в структуре анестезиологического обеспечения больных пожилого возраста при экстренных абдоминальных операциях. *Регионарная анестезия и лечение острой боли*, *5*(2), 14-21.
22. Кольга, А. Д., &Шарипов, Р. Х. (2010). Обоснование рациональных режимов эксплуатации выемочнопогрузочных машин. *Добыча, обработка и применение риродного камня: сб. науч. тр*, 181-184.
23. Rasulova, N. A., &Irbutaeva, L. T. (2021).THE EFFECTIVENESS OF NEBULIZER THERAPY IN BRONCHO-OBSTRUCTIVE CONDITIONS. *CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES*, *2*(3), 178-181.
24. Малышев, А. А., Свиридов, С. В., &Шарипов, Р. Х. (2015). Пролонгированная эпидуральная анальгезия в периоперационном периоде у больных при лапароскопических операциях на желудочно-кишечном тракте. *Регионарная анестезия и лечение острой боли*, *9*(4), 16-20.
25. Свиридов, С. В., Малышев, В. Д., Веденина, И. В., &Шарипов, Р. Х. (2009). Роль осмолярности и коллоидно-онкотического давления крови в поддержании жидкостного баланса. *Российский медицинский журнал*, (4), 49-53.
26. Шарипов, Р. Х. (2008). Перинатальные гипоксические неврологические синдромы (клиника, диагностика, лечение, прогноз).
27. Шарипов, Р. Х. (1994). Применение препаратов мембранотропного действия в

комплексном лечении недоношенных детей с перинатальной энцефалопатией. *Организационные и клинические проблемы детской неврологии и психиатрии: Тезисы докладов/Под ред. КА Семеновой и ОД Сосюкало.–М.: Издат-во АО "Руссомед*, *2*, 63-65.

28. Шарипов, Р. Х., Махмудова, З. Р., &Мамаризаев, И. К. (2021). ПОНИЖЕННЫЙ УРОВЕНЬ ВИТАМИНА Д КАК ФАКТОР РИСКА РАЗВИТИЯ АТОПИЧЕСКИХ ЗАБОЛЕВАНИЙ. *Научные исследования*, (1 (36)), 51-52.
29. ШАРИПОВ, Р. Х., РАСУЛОВА, Н. А., & МАХМУДОВА, З. Р. (2020). Новые горизонты, улучшающие соматический статус детей раннего возраста. *ЖУРНАЛ НЕВРОЛОГИИ И НЕЙРОХИРУРГИЧЕСКИХ ИССЛЕДОВАНИЙ*, *1*(2).
30. Артыкова, Н., &Музаффарова, Ф. (2019). Внешняя политика Узбекистана и социальное развитие. In *WORLD SCIENCE: PROBLEMS AND INNOVATIONS* (pp. 200-203).
31. Akramovna, O. N. (2021). Innovative Possibilities of Pedagogical Forecasting. *European Journal of Life Safety and Stability (2660-9630)*, *11*, 189-191.
32. Ortikova, N., &Rizaev, J. (2021, May). THE PREVALENCE AND REASONS OF STOMATOPHOBIA IN CHILDREN.In *Euro-Asia Conferences* (Vol. 5, No. 1, pp. 182-183).
33. Juraev, N., &Ortikova, N. (2021). THEORETICAL SOURCES OF THE CONCEPT OF THE POLITICAL ELITE: A COMPARATIVE ANALYSIS. *PalArch's Journal of Archaeology of Egypt/Egyptology*, *18*(7), 1953-1961.
34. Norbutaev, A., Rizaev, J., Abduvakilov, J., &Ortikova, N. (2020). Results of the effect of complex treatments on perodonot microcirculation in child periodontitis with iron deficiency. *European Journal of Molecular & Clinical Medicine*, *7*(2), 2020.
35. Ortikova, N. (2019). CHALLENGES TO SHAPE POLITICAL ELITE. In *Modern philosophic paradigms: interrelation of traditions and innovative approaches* (pp. 17-22).
36. Ortikova, N. (2018). THEORETICAL FOUNDATIONS OF POLITICAL ELITE AND DEMOCRACY. *Социосфера*, (4), 233-237.